



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Ibalizumab (IBA, Trogarzo) (Last updated April 14, 2020; last reviewed April 14, 2020)

Formulations

Single-Dose Vial for Intravenous Administration: 200 mg/1.33 mL (150 mg/mL) in a single-dose vial. Each single-dose vial contains the following inactive ingredients: L-histidine, polysorbate 80, sodium chloride, and sucrose.

Dosing Recommendations

Child and Adolescent Dose:

- The safety and efficacy of using ibalizumab (IBA) in children and adolescents has not been established.

Adult Dose:

- A single loading dose infusion of IBA 2,000 mg administered intravenously (IV) over 30 minutes is followed by a maintenance dose of IBA 800 mg administered IV over 15 minutes every 2 weeks.
- Food and Drug Administration approval of IBA is limited to heavily treatment-experienced adults with multidrug-resistant HIV infection who are experiencing treatment failure on their current regimen.
- IBA is used in combination with other antiretroviral drugs.

Selected Adverse Events

- Diarrhea, dizziness, nausea, rash
- Immune reconstitution inflammatory syndrome
- Potential for immunogenicity in the form of anti-IBA antibodies

Special Instructions

- The solution in the vial has to be diluted in 0.9% Sodium Chloride Injection and administered by IV infusion.
- Using aseptic technique, withdraw 1.33 mL from each vial and transfer into a 250 mL bag of 0.9% sodium chloride for IV injection. Other IV diluents must not be used.
- Once diluted, the solution should be administered immediately. If not used immediately, the solution can be stored at room temperature for up to 4 hours or refrigerated for up to 24 hours. Refrigerated solution should be allowed to stand at room temperature for at least 30 minutes but no more than 4 hours prior to administration.
- Diluted solution is administered as an IV infusion, not as a bolus or IV push.

Metabolism/Elimination

- Monoclonal antibodies are metabolized to peptides and amino acids.

Drug Interactions (see also the [Adult and Adolescent Antiretroviral Guidelines](#) and [HIV Drug Interaction Checker](#))

Ibalizumab (IBA) is a humanized IgG4 monoclonal antibody that blocks HIV entry into CD4 T lymphocytes (CD4). Based on IBA's mechanism of action and target-mediated drug disposition, drug-drug interactions are not expected. However, no drug interaction studies have been conducted.¹

Major Toxicities

- More common:* Rash, diarrhea, headache, nausea, dizziness, depression.^{1,2}
- Less common (more severe):* Immune reconstitution inflammatory syndrome.¹

Resistance

HIV has shown reduced susceptibility to IBA, as defined by a decrease in maximum percent inhibition, when HIV loses N-linked glycosylation sites in the V5 loop of glycoprotein 120.¹⁻³

Phenotypic and genotypic test results showed no evidence of cross resistance between IBA and any Food and Drug Administration (FDA)-approved classes of antiretroviral (ARV) drugs.⁴ IBA exhibits ARV activity against R5-tropic, X4-tropic, and dual-tropic HIV.⁴

Pediatric Use

Approval

IBA is not approved by the FDA for use in pediatric patients. IBA was approved by the FDA in 2018 for use in adults in combination with other ARV drugs, with approval limited to heavily treatment-experienced adults with multidrug-resistant HIV who are experiencing treatment failure on their current regimen.⁵

Efficacy in Clinical Trials

Trial TMB-301 was conducted in 40 adults aged 23 to 65 years who had body weights ranging from 50 kg to 130 kg, who had resistance to ARV drugs from three classes, who had been treated for at least 6 months on stable ARV regimens and had viral loads >1,000 copies/mL, and who had viral sensitivity to at least one ARV drug.^{3,5} Participants continued their current ARV regimens and received a 2,000-mg loading dose of IBA on Day 7 of the study. One week after the loading dose, participants optimized their ARV regimens. Participants received IBA 800 mg on Day 21 and every 2 weeks thereafter. At Week 25, 43% of participants achieved suppressed viral loads of <50 copies/mL.^{1,3} At Week 48 of an open-label extension study, 24 participants were taking IBA and their optimized ARV regimen. Sixteen of 27 participants (59%) had viral loads <50 copies/mL at 48 weeks.^{6,7}

Mechanism of Action

IBA is a recombinant humanized monoclonal antibody that blocks HIV from infecting CD4 cells. It does this by binding to domain 2 of the CD4 receptor, which interferes with the post-attachment steps that allow HIV virus particles to enter host cells and prevents the viral transmission that occurs via cell-cell fusion.^{1,7} Since IBA binds to a conformational epitope located primarily in domain 2 of the extracellular portion of the CD4 receptor, away from Major Histocompatibility Complex II molecule binding sites, it does not interfere with CD4-mediated immune functions.

References

1. Ibalizumab [package insert]. Food and Drug Administration. 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761065lbl.pdf.
2. Jacob SA, Jacob DG. Ibalizumab targeting CD4 receptors, an emerging molecule in HIV therapy. *Front Microbiol*. 2017;8:2323. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29230203>.
3. Emu B, Fessel J, Schrader S, et al. Phase 3 Study of ibalizumab for multidrug-resistant HIV-1. *N Engl J Med*. 2018;379(7):645-654. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30110589>.
4. Weinheimer S, Cohen Z, Marsolais C, Lewis S. Ibalizumab susceptibility in patient HIV isolates resistant to antiretrovirals. Abstract 561. Presented at: Conference on Retroviruses and Opportunistic Infections. 2018. Boston, Massachusetts. Available at: <http://www.croiconference.org/sessions/ibalizumab-susceptibility-patient-hiv-isolates-resistant-antiretrovirals>.
5. Food and Drug Administration. Drug approval package: Trogarzo injection (ibalizumab-uiyk). 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/TROGARZO_761065_TOC.cfm.
6. Emu B, Fessel J, Schrader S, et al. Forty-eight-week safety and efficacy on-treatment analysis of ibalizumab in patients with multi-drug resistant HIV-1. *Open Forum Infect Dis*. 2017;4(Suppl 1):S38-S39. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5632088/>.
7. Gulick RM. Investigational antiretroviral drugs: what is coming down the pipeline. *Top Antivir Med*. 2018;25(4):127-132. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29689540>.